draft CHARTER for a Collaborative Community on
Smart and Autonomous Medical Systems (SaAMS)

What are Smart and Autonomous Medical Systems (SaAMS)?
Smart and Autonomous Medical Systems (SaAMS) describe medical systems in which smart apps connect to medical devices to deliver transformative patient-care solutions safely and efficiently. SaAMS may use sophisticated algorithms that interact with interoperable medical devices to perform tasks that improve patient safety or efficiency, make decisions, automate processes, enhance vigilance, personalize patient and user experiences, advance healthcare equity, and solve historically intractable problems. These algorithms may be based on artificial intelligence (AI) to adapt to new information, make predictions, and operate autonomously.

Why are SaAMS Vital?
The demands of the COVID-19 public health emergency (PHE) provided one example of the need for SaAMS. The PHE drove a community of federal, industry and academic stakeholders to work together to rapidly advance autonomous medical device capabilities using intravenous infusion pumps and lung ventilators to enable hybrid virtual/in-person care models in diverse healthcare delivery environments. [1,2] Innovation initiatives such as these demonstrated that healthcare delivery can be transformed by applying automation technologies used in other domains. Solutions can range from lower levels of autonomy (such as adaptive cruise control, smart alarms, or guardrail dosing limits for intravenous medication pumps) to higher levels of autonomy (such as automated anesthesia). Integrating actuators, sensors, and smart clinical algorithms are the foundational components of these SaAMS. Solving long-standing gaps in clinical technology effectiveness and patient safety require SaAMS-based solutions.

Examples of SaAMS applications:
- Automated closed loop control of intravenous anesthesia (ACLIVA)
  Closed-loop intravenous sedation and anesthesia have wide-ranging clinical utility in intraoperative and ICU settings, and for military and civilian austere medical care. [3]
- Closed-loop blood pressure control:
  Research has shown that closed-loop vasopressor therapy in which vasopressor medication is infused to achieve a target arterial pressure range can minimize intraoperative hypotension and maintain SAP within 10% of the target range for >90% of the case time. [4]
- Closed-Loop Controlled Fluid Administration:
  “For fluid management and administration, the advantages of closed-loop technology are clear, especially in conditions that require precise care to improve outcomes, such as peri-operative care, trauma, and acute burn care.” [5]
- Remote IV Infusion Pump Control and Remote Lung Ventilator Control:
  Remote control can facilitate care of patients undergoing anesthesia/sedation in hazardous environments (e.g. presence of ionizing radiation for neuroimaging), in settings where the IV pump or the ventilator cannot be readily accessed due to distance (e.g. certain OR and interventional procedures), and in airborne infection isolation rooms to protect caregivers from infection and enforce protective (reverse) isolation (e.g. large surface-area burns). [6]
- AI-based predictive clinical analytics:
  Artificial intelligence (AI)-based predictive analytics can provide real-time clinical analytics and dynamic visualization of patient anesthetic state, and “use machine learning and other modern

statistical techniques to provide early warning of events of clinical deterioration such as sepsis, respiratory failure, [and] hemorrhage, and emergent intensive care unit (ICU) transfer." [7]

- Smart alarms that improve sensitivity to clinically significant events and enhance specificity to reduce non-actionable alarms and reduce alarm fatigue.

The Need for a SaAMS Collaborative Community:

A Collaborative Community can address challenging medical technology needs that no single manufacturer or other entity may be able to accomplish alone. This includes identifying and advancing key enabling device features and clinical system capabilities that address complex engineering and clinical challenges (e.g. external control of pumps, safe fallback modes of closed-loop systems). [8,9] We are forming a Collaborative Community, as described by the FDA, "to achieve common outcomes, solve shared challenges, and leverage collective opportunities" to advance the maturity, adoption, and clinical use of SaAMS to improve patient care. [10]

Participants in the SaAMS Collaborative Community will include a wide range of experts including manufacturers, clinicians, engineers, researchers, and the US FDA, to collaborate on the development of evidence to support safety. This safety framework is intended to provide precompetitive evidence for use in the regulatory process to de-risk commercial development and increase the safety, effectiveness, and clinical usability of these systems. It is anticipated that the framework will align with, and inform, applicable risk-management concepts, terminology, standards, and regulatory guidance.

Deliverables to be Considered:

Deliverables are focused on evidence to support the safety and efficacy of SaAMS.

- Concept(s) of operation of the SaAMS systems including descriptions of clinical scenarios to assure conceptual interoperability
- Description of system components, architecture, and the necessary device data and control commands to assure safe operation (aligned with Medical Device Interface Data Sheets) [11]
- Use-case specific best practices
- Safety Assurance Case(s) and a shared risk model [12]
- Considerations for implementation in Integrated Clinical Environments (ICE) on platforms with interoperable, externally-controllable actuators, sensors, and smart clinical algorithms [13,14]
- Data logging / black box recorder requirements for quality assurance [15]
- Test methods – failure modes, fallback state(s), interoperability, communication degradation
- White papers, presentations, publications, content for inclusion in industry consensus standards

SaAMS Collaborative Community Engagement and Governance Rules:

The Collaborative Community is being led by Massachusetts General Hospital, under the direction of Julian M. Goldman, MD. This is a pre-competitive working group in which the parties agree to develop, gather, and analyze non-proprietary information to create publicly sharable evidence to support safe and effective SaAMS. Participating experts will be expected to develop and review documents produced by and for the group for technical excellence, completeness (topics are covered in sufficient depth), and comprehensiveness (not leaving out any major issues). Confidential information offered for use by the Collaborative Community shall be identified as such and may be excluded unless made available publicly. Recommendations made by the Collaborative Community may not be reflective of all members. Participants may not engage in anti-competitive practices.

The Collaborative Community will function as a perpetual working group that may operate through subgroups or project groups. The Community will aim to meet virtually at least 1-2 times annually, with quarterly Steering Committee meetings to include updates from subgroups or project groups. The subgroups will meet virtually, as needed, and engage in communication via email. Steering Committee meetings will include updates from subgroups or project groups. The subgroups will meet virtually, as needed, and engage in communication via email. Additional unstructured meetings will be held as needed. Community documents, including meeting notes, will be stored on a secure web site freely accessible to members. The Steering Committee will include experts from diverse backgrounds to provide technical, strategic, and operational guidance.

Major decisions relating to project selection, deliverable prioritization, document release criteria, and similar matters will be informed by a verbal vote from the body of members present at the time of the meeting, or by electronic ballot. Each member shall have one vote on each matter presented to the Collaborative Community. No member may vote by proxy. Decisions shall be determined by two thirds majority and affirmed by the steering committee and Program Director. The Community will strive to adjudicate negative votes to achieve consensus. An informal voting approach via email may be used where appropriate. The Charter will be reviewed regularly by the Program Director and Steering Committee and amended as needed. The Program Director will have final say in any disputes.

Sponsorship and Resourcing:
The SaAMS Collaborative Community is sponsored by the Medical Device Plug-and-Play Interoperability & Cybersecurity ("MD PnP") research program and its Center for Smart and Autonomous Medical Systems (SaAMS) at the Massachusetts General Hospital Department of Anesthesia, Critical Care, and Pain Medicine. The "plug-and-play interoperability" envisioned at the time of the founding of the MD PnP program in 2004 by Dr. Goldman was intended to enable the development of Smart and Autonomous Medical Systems. [16] This Collaborative Community to advance SaAMS is a realization of that vision.

Funding to initiate the SaAMS Collaborative Community is being provided by the MGH Center for SaAMS. Activities of the Collaborative Community may be resourced through philanthropic donations, foundation and government grants, and other sources when aligned with the mission and financial guidelines of MGH.

Initial Projects and Working Groups: It is anticipated that the following project-related working groups and sub-groups will be formed initially or soon after inception of the Community:
1. ACLIVA – identification and documentation of current barriers to advancing ACLIVA, including,
2. Externally controllable IV infusion pumps – current barriers to marketing
3. Collaborative Community web site – stand up resources for communication and document storage
4. Cybersecurity applicable to SaAMS – strategic assessment and pathway to advancement
5. Risk management and safety considerations for SaAMS - safety requirements and test methods.

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References:

1. National Emergency Tele-Critical Care Network, https://mdpnp.mgh.harvard.edu/astra-portfolio/netccn/
2. AAMI Consensus Report AAMI/CR511:2020 - Emergency Use Guidance for Remote Control of Medical Devices
3. Closing the loop: automation in anesthesiology is coming. J Clin Monit Comput (2023). https://doi.org/10.1007/s10877-023-01077-3
4. Systolic Arterial Pressure Control Using an Automated Closed-Loop System for Vasopressor Infusion during Intermediate-to-High-Risk Surgery: A Feasibility Study. J Pers Med. 2022 Sep 21;12(10):1554. doi: 10.3390/jpm12101554.
5. Closed-Loop Controlled Fluid Administration Systems: A Comprehensive Scoping Review. J Pers Med. 2022 Jul; 12(7): 1168. Published online 2022 Jul 18. doi: 10.3390/jpm12071168
6. Demonstration of Remote Control of Ventilators and Infusion Pumps to Support Disaster Care, US Army TATRC YouTube Channel, https://www.youtube.com/watch?v=XWAHkE73LrY, accessed November 28, 2023
7. Beyond prediction: Off-target uses of artificial intelligence-based predictive analytics in a learning health system. `Learn Health Syst. 2023 Jan; 7(1): e10323. Published online 2022 Jun 23. doi: 10.1002/lrh2.10323
8. IEC 60601-1-10:2007, Medical electrical equipment Part 1-10: General requirements for basic safety and essential performance, collateral standard: Requirements for the development of physiologic closed-loop controllers. (Last reviewed and confirmed 2020)
9. Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology (2023) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-medical-devices-physiologic-closed-loop-control-technology
10. Collaborative Communities: Addressing Health Care Challenges Together, https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together
11. Applying Medical Device Informatics to Enable Safe and Secure Interoperable Systems: Medical Device Interface Data Sheets, DOI: 10.1213/ANE.0000000000004251
12. Introduction of Assurance Case Method and its Application in Regulatory Science (5/1/2019). https://www.fda.gov/media/125182/download
13. Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices (Final Guidance, 2017) https://www.fda.gov/media/95636/download
14. ANSI/AAMI 2700-1:2019. American National Standard: Medical Devices and Medical Systems - Essential Safety And Performance Requirements For Equipment Comprising The Patient-Centric Integrated Clinical Environment (ICE) - Part 1: General Requirements And Conceptual Model.
15. ANSI/AAMI 2700-2-1:2022 - Medical Devices and Medical Systems - Essential Safety and Performance Requirements for Equipment Comprising The Patient-Centric Integrated Clinical Environment (ICE): Part 2-1: Particular Requirements For Forensic Data Logging
16. MGH MD PnP Program home page https://mdpnp.mgh.harvard.edu/

SaAMS Collaborative Community *Project 2024_01:*

Development of a Safety Framework for Automated Closed-Loop IV Anesthesia (ACLIVA):
consensus risk model and test methods for use in the regulatory process

Note: This ACLIVA project document must be considered in the context of the SaAMS Collaborative Community charter.

ACLIVA Problem Statement:
Automated Closed Loop control of IntraVenous Anesthesia (ACLIVA) using smart physiological feedback was chosen as a SaAMS Collaborative Community Project because it has wide-ranging and highly desirable clinical utility including intraoperative and ICU applications in settings as diverse as austere military and civilian care, critical access, and tertiary medical centers. [1] ACLIVA system components include clinical monitors (such as brain-state and vital signs monitors) that provide input to the PCLC system, and externally controllable infusion pumps (and potentially ventilators) that may be used as components of the system. Several ACLIVA products are available or under development on the global medical market, but ACLIVA is not available today in the US due to regulatory uncertainty, lack of consensus on engineering arguments for safety, and test methods to demonstrate effective risk control measures.

<u>ACLIVA requires:</u>
- Physiological sensors, such as processed EEG and cardiopulmonary monitors.
- Physiologic closed-loop control algorithms to autonomously "close the loop" between delivered medications and the desired (target) physiological state,
- Externally (remotely) controllable infusion pumps, and
- Remotely controllable ventilators (anticipated for some applications of ACLIVA).

Currently available infusion pumps, ventilators, and physiological sensors have limited to no remote-control capabilities and are not typically interoperable. Therefore, addressing these gaps is essential to the success of this initiative.

ACLIVA are complex systems, as such, this Project may spawn separate work streams such as:
- Medical Device Informatics related to medical device command and control:
    - Selection and analysis of data communication patterns and quality of service requirements for reliable medical device control
    - Nomenclature to support interoperability of IV pump control commands
    - Requirements to achieve functional safety of networked systems that require high levels of safety and reliability for SaAMS
- Hardware-in-the-loop testbeds for ACLIVA device interface, component, and system testing
- Guidelines and test methods for demonstrating equivalency for interoperable sensors, actuators, and applications

Objectives:

Developing a consensus safety framework to address the integration and performance of these components is necessary to assure the safety of ACLIVA and advance the US availability of these technologies for clinical care. The SaAMS Collaborative Community will collaborate on the development of a shared safety framework, risk model, and test methods to verify effective performance and risk-control measures for physiologic closed-loop control (PCLC) based Intravenous anesthesia systems. The safety framework is intended to provide precompetitive evidence to support safety and efficacy for use in the regulatory process to de-risk commercial development and increase the safety and clinical usability of these systems. The framework will align with applicable risk-management concepts and terminology, standards, and regulatory guidance:

- Standard IEC 60601-1-10 Requirements for the development of physiologic closed-loop controllers [2]
- Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology (Final Guidance, 2023) [3]
  - Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices (Final Guidance, 2017) [4]

Planned Deliverables:

- Concept(s) of operation of ACLIVA systems including descriptions of clinical scenarios to assure conceptual interoperability
- Description of system components, architecture, and the necessary device data and control commands to assure safe operation (aligned with Medical Device Interface Data Sheets [5])
- Safety Assurance Case(s)
- Data logging requirements [6]
- Test methods – failure modes, fallback state(s), interoperability, communication degradation
- White papers, presentations, publications, content for inclusion in consensus standards

References:

1. Coeckelenbergh, S., Joosten, A., Cannesson, M. et al. Closing the loop: automation in anesthesiology is coming. J Clin Monit Comput (2023). https://doi.org/10.1007/s10877-023-01077-3
2. IEC 60601-1-10:2007, Medical electrical equipment Part 1-10: General requirements for basic safety and essential performance, collateral standard: Requirements for the development of physiologic closed-loop controllers. (Last reviewed and confirmed 2020)
3. Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology (2023) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-medical-devices-physiologic-closed-loop-control-technology
4. Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices (Final Guidance, 2017) https://www.fda.gov/media/95636/download
5. Applying Medical Device Informatics to Enable Safe and Secure Interoperable Systems: Medical Device Interface Data Sheets, DOI: 10.1213/ANE.0000000000004251
6. ANSI/AAMI 2700-2-1:2022 - Medical Devices and Medical Systems - Essential Safety and Performance Requirements For Equipment Comprising The Patient-Centric Integrated Clinical Environment (ICE): Part 2-1: Particular Requirements For Forensic Data Logging